REMARKS

Claims 79-90 are pending in the subject application. Applicants have hereinabove cancelled claims 80, 82 and 83 without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in the future. In addition, applicants have amended claims 79 and 81. Support for the amendments to claim 79 can be found in the specification as originally filed at, inter alia, page 7, lines 4-10; page 9, lines 9-11 and 30-32; page 18, lines 1-5; page 40, lines 29-31; page 41, lines 7-27; and page 3, line 13 which indicates "CFU-F" is an abbreviation for "colony-forming-unit-fibroblasts". Support for the amendments to claim 81 can be found in the specification as originally filed at, inter alia, page 1, lines 7-11; page 13, lines 14-21; page 6, lines 11-13; page 43, line 28 to page 44, line 10; page 12, lines 25 to 31; and at page 14, lines 27 to 32.

Applicants maintain that the amendments made hereinabove raise no issue of new matter. Accordingly, applicants respectfully request entry of this Amendment.

Claims Rejected Under 35 U.S.C. §112, first paragraph (written description)

In the October 19, 2007 Office Action the Examiner stated that claim 79 and those dependent therefrom are rejected under 35 U.S.C. §112, first paragraph (written description), asserting that the specification and claims as originally filed only support a method of enriching for MPCs, and for a subpopulation of STRO-1^{bright} cells in particular.

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that, besides the support specified in the Remarks section above, the specification describes at page 18, lines 1-5:

> "In a further form the invention might be said to reside a method of generation tissue in a mammal comprising the step of enriching a population of precursor cells as in the first aspect of the invention, and introducing the enriched population into the mammal, and allowing the enriched population to generate the tissue in the mammal."

Support is also provided at page 1, lines 20-21 where the specification states:

> "Purification or at least enrichment of MPCs is desirable for a variety of therapeutic reasons. The reasons include regeneration of missing or damaged skeletal tissue..."

It is additionally provided in the specification at page 7, lines 17 and 18 that for the enriched population:

> "at least one of the markers is the antigen recognised by STRO-1, and in particular the high level of expression of that antigen."

The culture expanded bulk CFU-F derived from STRO-1^{bright}/VCAM-1^{+} sorted cells are described at page 40, line 29, and page 3, line 13 indicates "CFU-F" is an abbreviation for "colony-forming-unit-fibroblasts".

Applicants thus maintain that the invention as claimed is clearly described in the specification as originally filed so as to reasonably convey to one of ordinary skill in the art that applicants had possession of the invention as claimed. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims Rejected Under 35 U.S.C. §112, first paragraph (enablement)

In the October 19, 2007 Office Action the Examiner stated that claim 79 and those dependent therefrom are rejected under 35 U.S.C. §112, first paragraph (enablement), asserting that the specification does not enable one of ordinary skill in the art to practice the invention without an undue amount of experimentation. The Examiner stated that the specification only discloses a detailed *in vitro* method for isolation and purification of SRTO-1^{bright} BM MPC. The Examiner stated that the specification further disclosed *in vitro* studies of possible chrondrogenic potential of said SRTO-1^{bright} BM MPC. The Examiner stated, however, that the specification explicitly states that within SRTO-1^{bright}/VCAM-1^{bright} BM fraction there are several additional sub-fractions that might have different developmental potential (see pages 32 in particular).

The Examiner further stated that the specification does not adequately teach how to effectively generate any mesenchymal tissue in any subject, including humans by administering a population of STRO-1^{bright} cells. The Examiner, moreover, stated that no animal models were used to study the effectiveness of generating any mesenchymal tissue in any subject, including humans by administering a population of STRO-1^{bright} cells. The Examiner also stated that since there are no animal model studies and data in the specification to show the effectiveness of generating any mesenchymal tissue in any subject, including humans by administering a population of STRO-1^{bright} cells, it is unpredictable how to correlate *in vitro* results with *in vivo* uses. The Examiner stated that the specification does not teach how to extrapolate data obtained from *in vitro* studies to the

development of effectiveness *in vivo* mammalian therapeutic treatment, commensurate in scope with the claimed invention.

The Examiner further stated that although the specification describes several in vitro data, there is no correlation on this record between the said results and a claimed method of generating any mesenchymal tissue in any subject by administering STRO-1^{bright} cells in currently available form for humans or animals. The Examiner stated that it is not enough to rely on *in vitro* studies where, as here, a person having ordinary skill in the art has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to efficacy in humans or animals.

Applicants' Reply

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that the application does in fact provide *in vivo* data on generation of a tissue. Applicants respectfully direct the Examiner's attention to page 41, line 7 to page 42, line 4. Therein is described a mouse model in which expanded human cells from a population enriched for STRO-1^{bright} were implanted subcutaneously. Blood vessels and fibrous tissue was found in the implants and bone was formed (see Fig. 8). The bone lining cells, fibrous tissue and osteocytes within the newly formed bone were all identified "being positive for the alu sequence confirming their human origin", page 41, lines 31-33. In addition, the method stimulated generation of endogenous tissue such as fat and smooth muscle (see page 41, lines 34-36). Furthermore, Examples 2 through 4 on page 42 provide further guidance as to generating tissue using the claimed method.

Accordingly, applicants maintain that, contrary to the Examiner's position, the specification provides *in vivo* data for the claimed method. Applicants further maintain that one of ordinary skill in the art, based on the teachings of the specification, would be able to make and use the invention as claimed. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the items listed below which are also listed on the Substitute PTO-1449 form attached hereto as **Exhibit A**.

Items 1-3 are U.S. Patent application publications. No copies of these items are enclosed as permitted by 37 C.F.R. §1.98(2)(ii). Copies of items 4-35 are attached hereto as **Exhibits 1-32**, respectively. Applicants note that items 4-8, 34 and 35 are Office Actions issued in related U.S. applications.

1. U.S. Patent Application Publication No. 2007-0065938 A1 published March 22, 2007;
2. U.S. Patent Application Publication No. 2006-0286077 A1 published December 21, 2006;
3. U.S. Patent Application Publication No. 2006-0193840 A1 published August 31, 2006;
4. Office Action issued August 25, 2006 in connection with U.S. Serial No. 10/955,709; **(Exhibit 1)**
5. Office Action issued August 24, 2007 in connection with U.S. Serial No. 11/178,920; **(Exhibit 2)**
6. Office Action issued December 15, 2006 in connection with U.S. Serial No. 11/178,920; **(Exhibit 3)**
7. Office Action issued July 10, 2006 in connection with U.S. Serial No. 11/178,920; **(Exhibit 4)**
8. Office Action issued January 22, 2007 in connection with U.S. Serial No. 11/169,875; **(Exhibit 5)**
9. Shi S et al: "Perivascular niche of postnatal mesenchymal stem cells in human bone marrow and

dental pulp." Journal of Bone and Mineral Research, vol. 17, no. Suppl 1, September 2002 (2002-09), page S446, XP009083412 & Twenty-Fourth Annual meeting of the American Society for Bone and Mineral Research; San Antonio, Texas, USA; September 20-24, 2002; **(Exhibit 6)**

10. Gronthos S et al: "Postnatal human dental pulp stem cells (DPSCs) in vitro and in vivo." Proceedings of the National Academy of Sciences of USA, National Academy of Science, Washington, DC, US, vol. 97, no. 25, 5 December 2000 (2000-12-05), pages 13625-13630; **(Exhibit 7)**
11. Shi S et al: "Perivascular niche of postnatal mesenchymal stem cells in human bone marrow and dental pulp." Journal of Bone and Mineral Research, New York, NY, US, vol. 18, no. 4, April 2003 (2003-04), page 696-704; **(Exhibit 8)**
12. Tse H F et al: "Angiogenesis in ischaemic myocardium by intramyocardial autologous bone marrow mononuclear cell implantation." Lancet The, Lancet Limited, London, GB, vol. 361, no. 9351, 4 January 2003 (2003-01-04), pages 47-49; **(Exhibit 9)**
13. Zvaifler, et al., (2000) "Mesenchymal precursor cells in the blood of normal individuals," Arthritis Research and Therapy, 2: 477-488; **(Exhibit 10)**
14. Ji, et al., (2004) "Interactions of Chemokines and Chemokine Receptors Mediate the Migration of Mesenchymal Stem Cells to the Impaired Site in the Brain After Hypoglossal Nerve Injury," Stem Cells, 22: 415-427; **(Exhibit 11)**
15. Sordi, et al., (2005) "Bone marrow mesenchymal

stem cells express a restricted set of functionally active chemokine receptors capable of promoting migration to pancreatic islets," Blood, 106(2): 419-427; **(Exhibit 12)**

16. Wynn, et al., (2004) "A small proportion of mesenchymal stem cells strongly expresses functionally active CXCR4 receptor capable of promoting migration to bone marrow," Blood, 104(9): 2643-2645; **(Exhibit 13)**
17. Kortesidis, et al., (2005) "Stromal-derived factor-1 promotes the growth, survival, and development of human bone marrow stromal stem cells," Blood, 105(10): 3793-3801; **(Exhibit 14)**
18. Gronthos, S., et al., (1999) "Differential Cell Surface Expression Of The STRO-1 And Alkaline Phosphatase Antigens On Discrete Developmental Stages In Primary Culture Of Human Bone Cells," Journal of Bone and Mineral Research, 14(1): 47-56; **(Exhibit 15)**
19. Stewart, K., et al., (1999) "Further Characterization Of Cells Expressing STRO-1 In Cultures Of Adult Human Bone Marrow Stromal Cells," Journal of Bone and Mineral Research, 14(8): 1345-1356; **(Exhibit 16)**
20. Supplementary European Search Report from European Patent Office, Application No. EP 04 72 3935, 10 May 2007; **(Exhibit 17)**
21. Supplementary European Search Report from European Patent Office, Application No. EP 04 72 3937, 25 May 2007; **(Exhibit 18)**
22. International Search Report issued by the

International Searching Authority (ISA/AU) on May 17, 2004 in connection with International Application No. PCT/AU2004/000416; **(Exhibit 19)**

23. International Preliminary Report on Patentability issued May 17, 2004 in connection with International Application No. PCT/AU2004/000416; **(Exhibit 20)**
24. International Publication No. WO 2001/004268 A1, MEDVET SCIENCE PTY LTD, published January 18, 2001; **(Exhibit 21)**
25. International Search Report issued by the International Searching Authority (ISA/AU) on May 17, 2004 in connection with International Application No. PCT/AU2004/000417; **(Exhibit 22)**
26. International Preliminary Report on Patentability issued by the International Bureau of WIPO on October 1, 2005 in connection with International Application No. PCT/AU2004/000417; **(Exhibit 23)**
27. International Search Report issued by the International Searching Authority (ISA/AU) on August 22, 2005 in connection with International Application No. PCT/AU2005/000953; **(Exhibit 24)**
28. International Search Report issued by the International Searching Authority (ISA/AU) on November 25, 2005 in connection with International Application No. PCT/AU2005/001445; **(Exhibit 25)**
29. U.S. Serial No. 11/663,570, filed March 23, 2007; **(Exhibit 26)**
30. U.S. Serial No. 11/663,563, filed March 23, 2007; **(Exhibit 27)**
31. PCT International Publication No. WO 1999/003973

A, Osiris Therapeutics Inc., published January 28, 1999; **(Exhibit 28)**

32. PCT International Publication No. WO 04/84921 A1, published October 7, 2004 (MEDVET SCIENCE PTY LTD and ANGIOBLAST SYSTEMS INCORPORATED); **(Exhibit 29)**
33. PCT International Publication No. WO 04/85630 A1 published October 7, 2004 (MEDVET SCIENCE PTY LTD and ANGIOBLAST SYSTEMS INCORPORATED); **(Exhibit 30)**
34. Office Action issued January 8, 2008 in connection with U.S. Serial No. 11/326,736; **(Exhibit 31)** and
35. Office Action issued January 8, 2008 in connection with U.S. Serial No. 11/326,736. **(Exhibit 32)**

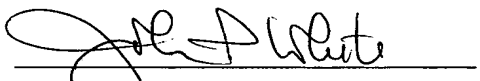
This Supplemental Information Disclosure Statement is being submitted under 37 C.F.R. §1.97(c)(2). Accordingly, applicants enclose a check in the amount of ONE HUNDRED AND EIGHTY DOLLARS for filing this Supplemental Information Disclosure Statement.

The Examiner is respectfully requested to make the listed items of record in the present application by initialing and returning a copy of the enclosed Substitute Form PTO 1449.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed $180.00 Information Disclosure Statement fee necessary in connection with the filing of this Amendment and Supplemental Information Disclosure Statement. However, if any additional fee is required authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

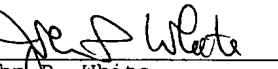
Respectfully submitted,



John P. White
Registration No. 28,678
Attorney for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.



11/22/08

John P. White Date
Reg. No. 28,678